IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Appl. No.	:	10/680,950	Confirmation No. 6033
Applicant	:	Robert Langley	
Filed	:	October 8, 2003	
TC/A.U.	:	3761	
Examiner	:	DEAK, Leslie R	
For	:	METHODS AND DEVICES FOR PROCESSING BLOOD	
Docket No.	:	96-03	
Customer No.	:	23713	

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August 7, 2008 /michaelcurtis/
Date Michael Curtis

APPEAL BRIEF

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Commissioner for Patents
P.O. Box 1450
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Sir:

A Notice of Appeal and a request for a Pre-Appeal Brief Conference for the application identified above were filed on April 18, 2008. The Patent Office issued a Notice of Panel Decision from pre-Appeal Brief Review on June 9, 2008 maintaining all rejections. This Appeal Brief is hereby submitted to provide support for patentability and to request allowance of all pending claims.

I. REAL PARTY IN INTEREST

The Real Party of Interest for this application is CaridianBCT, Inc., formerly known as Gambro BCT, Inc., 10811 West Collins Avenue, Lakewood, Colorado 80215.

II. RELATED APPEALS AND INTERFERENCES

There are no prior or pending appeals, interferences or judicial proceedings that are related to the pending appeal.

III. STATUS OF CLAIMS

Claims 1-53 and 56-68 are pending in this application. Claims 54 and 55 have previously been canceled. By means of the final Office Action issued on January 18, 2008, claims 1-53 and 56-68 were rejected and are presently appealed. The claims were last amended in the Amendment and Response filed on April 11, 2007 and are listed in the Claims Appendix attached hereto.

IV. STATUS OF AMENDMENTS

No amendments to the claims have been filed subsequent to the final rejection.

V. SUMMARY OF CLAIMED SUBJECT MATTER

The claimed invention is in the field of blood apheresis where blood removed from a subject is passed through an apparatus that separates and collects a particular blood component and returns the remaining blood components back to the subject's circulatory system. There are three independent claims, claims 25, 26 and 27, drawn to methods of processing blood from a subject. General description of the blood processing procedure and the corresponding device can be found on page 5, lines 7-30; page 22 through page 23; and Figure 1 of the specification as filed. Blood is removed and returned through a blood vessel accessed by a needle. In some embodiments the same needle and blood vessel are used for removing and returning blood, but in some embodiments different needles and blood vessels may be used for removing and returning blood. Blood is removed from a subject at a selected removal flow rate, processed so that one or more blood components, such as platelets, white blood cells or plasma, are collected from the removed blood, and the remaining blood components returned to the subject at a selected return flow rate. Furthermore, the total blood volume of the subject is determined and the blood removal flow rate, blood return flow rate, or both are adjusted during operation of the blood processing procedure according

to the total blood volume in order to prevent patient discomfort and blood vessel infiltration due to pressure changes in the accessed blood vessel during the removal or return of blood. The invention as claimed is further described in the specification on page 7, line 4, through page 8, line 2; and page 31, line 16, through page 32, line 4.

Specifically, independent claim 25 is to a method comprising determining the total blood volume of the subject; removing blood from the subject at a selected rate, where the blood removal flow rate is adjusted during operation of the blood processing procedure based on the subject's total blood volume; processing the removed blood; and returning the blood to the subject (page 7, lines 28-30, of the specification).

Independent claim 26 is to a method comprising determining the total blood volume of the subject; removing blood from the subject; processing the removed blood; and returning the blood to the subject at a selected return flow rate, where the blood return flow rate is adjusted during operation of the blood processing procedure based on the subject's total blood volume (page 7, lines 28-30).

Independent claim 27 is to a method comprising determining the total blood volume of the subject; removing blood from the subject at a selected rate, where the blood removal flow rate is adjusted during operation of the blood processing procedure based on the subject's total blood volume; processing the removed blood; and returning the blood to the subject at a selected return rate, where the blood return flow rate is adjusted during operation of the blood processing procedure based on the subject's total blood volume (page 7, lines 28-30).

Claim 1 is a dependent claim where the blood return flow rate is systematically varied over the return time. Similarly, claim 11 is a dependent claim where the blood removal flow rate is systemically varied over the removal time, and claim 23 is a dependent claim where the blood return rate is systemically decreased. Page 19, lines 8-12, of the specification as filed defines "systemically varying" as being varied by "substantially linear variations, exponential variations, logarithmic variations, quadratic

variations". Claims 3, 8 and 9 depend from claim 1 and specifically recite that the blood return rate decreases in a substantially linear manner or exponentially over the return time. Claim 10 also depends from claim 1 and recites that the return flow rate increases over the return time. These claims are further described on page 5, lines 7-23, and pages 16-19 of the specification.

Claim 4 is a dependent claim where the blood return flow rate is provided by the equation: $Z_{ret} = [F_0 + 2(1- F_0)(t/t_r)] Q_{ret}$; wherein Z_{ret} is said return flow rate, t is time, F_0 has a value greater than 1 and less than or equal to 2, t_r is said return time and Q_{ret} is an average return flow rate. Claims 5-7 depend from claim 4 and recite values for the variables in claim 4, such as Q_{ret} and t_r. These claims are described on page 25, lines 7-25, of the specification.

Claim 30 is a dependent claim where the blood removal rate is provided by the equation: $Z_{rem} = (M_{rem}) \times (V_B) \leq Q_{rem\ max}$, wherein Z_{rem} is the removal flow rate, M_{rem} is a removal flow rate slope, V_B is the total blood volume of said subject and $Q_{rem\ max}$ is a maximum removal flow rate. This claim is generally described on page 27, line 25, through page 28, line 26, where M_{rem} is $(C_{qi}) \times (A_{rem})$. Claims 34, 35 and 38 depend from claim 30 and recite values for the variables in claim 30, such as $Q_{rem\ max}$.

Claim 31 is a dependent claim where the blood return rate is provided by the equation: $Z_{ret} = (M_{ret}) \times (V_B) \leq Q_{ret\ max}$, wherein Z_{ret} is the return flow rate, M_{ret} is a return flow rate slope, V_B is the total blood volume of said subject, and $Q_{ret\ max}$ is a maximum return flow rate. This claim is generally described on page 27, line 25, through page 28, line 26, where $M_{ret} = (C_{qr}) \times (A_{ret})$. Claims 36, 37 and 39 depend from claim 31 and recite values for the variables in claim 31, such as $Q_{ret\ max}$.

Claim 59 is a dependent claim where the fraction by volume to be collected by the blood processing device is designated by the variable F_{cmax} and is provided by the equation:

$$F_{c\max} = \left(\left(\left[A^2 + \frac{(1-b)}{(1-D)} \right]^{0.5} - A \right) \right), \text{ wherein } b = \frac{H_{rem}}{H_{recir}}.$$

Claims 60-62 depend from claim 59 and recite values for the variables in claim 59. This claim is generally described on page 33, line 16, through page 36, line 12.

Claim 68 is a dependent claim where the fraction by volume to be collected by the blood processing device is designated by the variable F_{cmax} and is provided by the equation:

$$F_{c\max} = \left(\frac{\left(\left[A^2 + \frac{(1-z)(1-b)}{(1-D)} \right]^{0.5} - A \right)}{(1-z)} \right), \text{ wherein } b = \frac{H_{rem}}{H_{recir}}.$$

This claim is described on page 33, line 16, through page 36, line 12.

VI. GROUNDS OF REJECTION TO BE REVIEWED ON APPEAL

1. In the final Office Action issued January 18, 2008, the Examiner rejects claims 1-12, 14-15, 17-40, 42-45, 47-50 and 67 under 35 U.S.C. §103(a) as being obvious over U.S. Patent 6,179,801 (herein referred to as "Holmes") in view of U.S. Patent 5,980,465 (herein referred to as "Elgas"). These rejections encompass independent claims 25-27.

The Examiner states that Holmes discloses a blood processing device where total blood volume of the patient is used to determine various parameters of the apheresis procedure. Specifically, the Examiner asserts that the blood removal pump (reference number 1030) and blood return pump (reference number 1090) of Holmes are operated according to the predetermined operating protocol of the blood processing device, where the operating protocol operates, in part, on patient blood volume data (page 2, lines 10-21, of the January 18th Office Action). The Examiner admits that Holmes fails to disclose the steps of adjusting the blood removal flow rate and blood

return flow rate during the blood processing procedure based on the total blood volume (page 3, lines 3-4, of the January 18th Office Action.) However, the Examiner asserts this deficiency is overcome by the combination with Elgas.

The Examiner states that Elgas discloses that maintaining a patient's total blood volume is clinically significant to the patient's physiological status, and teaches that administering an outside fluid to the patient in the event of a decrease in total blood volume is a good way to maintain the patient's status quo (page 3, lines 4-10, of the January 18th Office Action). The Examiner asserts that the disclosure in Elgas therefore reasonably suggests that other steps, such as adjusting the blood withdrawal rate of the device, could also be used to maintain the patient's total blood volume (page 3, lines 10-12, of the January 18th Office Action). The Examiner then concludes that it would have been obvious to one skilled in the art to use the suggestion of Elgas, with regard to maintaining total blood volume through fluid flow rate adjustments, with the procedure in Holmes to arrive at the claimed invention.

2. With regard to claims drawn to "systemic" variations of the flow rates (claims 1, 11 and 23), the Examiner further asserts that Holmes clearly discloses that the apheresis system varies the flow rates based on a predetermined operating scheme (page 3, lines 18-21, of the January 18th Office Action). Since the apheresis system disclosed in Holmes controls such variations, the Examiner concludes the flow rates adjusted by the apheresis system correspond to Applicants' "systemic" variations (page 3, line 21, through page 4, line 2, of the January 18th Office Action).

3. With regard to claims 3, 8, 9 and 10, the Examiner further states that Holmes discloses patient data, such as total blood volume, which is used to establish the operating parameters of the apheresis device (page 5, lines 8-11, of the January 18th Office Action). The Examiner then states that Holmes teaches that the volume transfer rate of blood flow is a variable based on a predetermined protocol of the apheresis device. Therefore, the Examiner concludes the blood flow rate is a result-effective variable under MPEP 2144.05. The Examiner states that the optimization of a result-

effective variable involves only routine skill in the art, and considers the variable flow rates in the present claims (e.g., increasing, decreasing, exponentially decreasing, or linearly varying) to be a result-effective variable, the adjustment of which does not patentable distinguish over the prior art of record (page 5, lines 11-20, of the January 18th Office Action).

4. With regards to claims 4-7, 30-31 and 34-39, the Examiner notes that the blood flow rates in these claims are based on specific equations. As discussed above, the Examiner asserts that Holmes discloses the use of patient data to establish the operating parameters of the apherisis device, and that the volume transfer rate of blood flow is variable based on a predetermined protocol of the apherisis machine. Therefore, the Examiner asserts the flow rate is a result-effective variable (page 5, lines 8-20, of the January 18th Office Action). "Absent a disclosure that Applicant's claimed equations provide a significant advantage over the prior art's calculation, Examiner considers the selection of such variable parameters to be mere optimization of a result-effective variable through routine experimentation. Holmes specifically teaches that such parameters may be selected as desired by the operator and blood handling procedure (see, generally, columns 27-28). Accordingly, as previously noted, the optimization of a variable flow rate is not considered to patentably distinguish Applicant's invention from the prior art of the record. See MPEP 2144.05." (page 6, lines 3-10, of the January 18th Office Action).

5. The Examiner also rejects claims 59-62 and 68 under 35 U.S.C. §103(a) as being obvious over Holmes in view of Elgas, further in view of U.S. Patent 6,730,054 (herein referred to as "Pierce"). Pierce describes a blood processing procedure and device where blood is removed from a donor, recirculated through the device, and the desired blood components separated and collected.

With regards to claims 59-62 and 68, which disclose specific equations for determining the proper blood fraction for collection based, in part, on cycle duration and the hematocrit ratio between the removed blood and recirculated blood, the Examiner

states that each portion of blood necessarily has a hematocrit value, and that the draw and return cycles of Holmes and Pierce have a rate (page 11, lines 12-17, of the January 18th Office Action). The Examiner further concludes that all of the values used in the equations are demonstrated by the prior art to be variable and concludes these claims are therefore merely the optimization of a result-effective variable under MPEP 2144.05 (page 11, lines 17-20, of the January 18th Office Action).

VII. ARGUMENTS

1. Claims 1-12, 14-15, 17-40, 42-45, 47-50 and 67 rejected under 35 U.S.C. §103(a) as being obvious over Holmes in view of Elgas

This ground of rejection encompasses independent claims 25-27. All other pending claims ultimately depend from one of these three independent claims. Therefore, it is appropriate to argue the general patentability of the claims for this ground of rejection based on these independent claims. Specifically, claim 25 recites a method of processing blood comprising "removing blood from said subject at a selected removal flow rate thereby generating removed blood, wherein said selected removal flow rate is adjusted during operation of the blood processing procedure based on said total blood volume." Claim 26 recites a method of processing blood comprising "returning at least a portion of said return component to said subject at a selected return flow rate, wherein said selected return flow rate is adjusted during operation of the blood processing procedure based on said total blood volume of said subject." Claim 27 contains both limitations and requires that both the blood removal flow rate and return flow rate are adjusted during operation of the blood processing procedure based on the total blood volume. Applicants believe the Examiner has failed to make a proper prima facie case of obviousness in light of Holmes in combination with the suggestion provided by Elgas, and appeal this ground of rejection.

Holmes discloses a blood apheresis system where blood is removed from a patient, processed, and a portion of the blood returned to the patient. However, as acknowledged by the Examiner, Holmes does not adjust the blood removal flow rate or blood return flow rate based on the total blood volume (page 3, lines 3-4, of the January 18th Office Action). The Examiner tries to rectify the deficiencies of Holmes through the combination with Elgas.

The Examiner asserts that Elgas discloses that maintaining a patient's total blood volume is clinically significant to the patient's physiological status, and teaches that administering fluid to the patient can be used in the event of a decrease in total blood volume (page 3, lines 4-10, of the January 18th Office Action). It should be noted that Elgas does not alter the blood removal flow rate or return flow rate of the blood processing device, but only teaches administration of outside IV fluids, blood transfusions or vasoconstricting medication as means for correcting low patient blood volume (column 1, lines 31-57, of Elgas). Nonetheless, the Examiner concludes that the disclosure in Elgas reasonably suggests that other steps, such as adjusting the blood withdrawal rate of the device, could also be used to maintain the patient's total blood volume (page 3, lines 10-12, of the January 18th Office Action). The Examiner then concludes that it would have been obvious to one skilled in the art to use the suggestion of Elgas with the procedure in Holmes to arrive at the claimed invention. Applicants respectfully disagree.

The key to supporting a rejection under 35 U.S.C. 103 is the clear articulation of the reasons why the claimed invention would have been obvious (MPEP 2141 and MPEP 2142). The Supreme Court in KSR International Co. v. Teleflex Inc., 550 U.S. ___, 127 S. Ct. 1727, 82 USPQ2d 1385, 1396 (2007) noted that the analysis supporting a rejection under 35 U.S.C. 103 should be made explicit. The Federal Circuit has stated that "rejections on obviousness cannot be sustained with mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." In re Kahn, 441 F.3d 977, 988, 78 USPQ2d 1329, 1336 (Fed. Cir. 2006). Applicants submit that the

Examiner has not provided clear, articulated reasoning that ultimately supports why one skilled in the art would rationally find the present claims obvious in light of Holmes and the steps disclosed in Elgas.

The Examiner's assertion that the patient's total blood volume could be maintained by adjusting the blood removal flow rate or blood return flow rate of the device is not supported by the disclosure in Elgas. Elgas discloses a method of tracking a patient's blood volume during cardiac surgery where a heart-lung machine drains blood from the patient, oxygenates the blood, and pumps the blood back to the patient (column 1, lines 18-67, of Elgas). The patient's blood volume is monitored through the use of a marker substance injected into the patient's bloodstream. If the blood volume in the patient's circulatory system is too low, corrective steps, such as the administration of intravenous fluids, blood transfusions or blood vessel constricting medication, can be taken to stabilize the blood volume (column 1, lines 43-47, of Elgas). However, it should be emphasized that the patient's blood volume is not adjusted by increasing the blood return flow rate or decreasing the blood removal flow rate of the heart-lung machine in Elgas. Nowhere does Elgas disclose adjusting the blood return flow rate or removal flow rate of the device itself. Thus, even if one skilled in the art were to combine the teachings in Holmes and Elgas, the result would not lead to the methods as presently claimed. Specifically, the combination of Elgas and Holmes does not result in adjusting the blood removal flow rate or return flow rate of the device during operation of the blood processing procedure as required by the present claims.

This argument was presented in the Response to Office Action file by Applicants on November 14, 2007. In response to Applicants' arguments, the Examiner states that "Elgas specifically teaches that the circulatory fluid of the patient (consisting of blood and IV fluids) is removed from the vena cave [sic] via a *variable speed roller pump*, indicating that the Elgas device is capable of varying fluid removal rate from the patient (see column 2, lines 40-48)," (cited on page 12, lines 13-16 of the January 18th Office Action). This, however, is a factual error. Column 2, lines 40-48, of Elgas states that blood is diverted from the vena cava by a cardiac pump 17 through a cardiotomy filter

19, into a venous reservoir 20. The variable-speed roller pump 22 referenced by the Examiner is not used to withdraw blood from the patient, but is used to move blood from the reservoir 20 to the oxygenation unit 24 after the blood has already been removed from the patient (column 2, lines 44-47, of Elgas). There is no disclosure that the cardiac pump is used to, or is even able to, vary the blood removal rate, and hence Elgas cannot fairly be interpreted to disclose or suggest a blood processing method wherein the blood removal flow rate or return flow rate is adjusted during processing, let alone adjusted based on the total blood volume.

The Examiner concedes that Elgas does not disclose adjusting the blood removal flow rate or return flow rate of the device and states "the Examiner is not relying on the Elgas reference to teach the variation of blood removal and/or return rates," (page 12, lines 17-18, of the January 18th Office Action). Instead, the Examiner states that Elgas is being used to merely illustrate that patient blood volume is one of many patient parameters used to control an extracorporeal procedure (page 13, lines 1-5, of the January 18th Office Action). In light of the Examiner's previous acknowledgement that Holmes does not teach adjusting the blood removal or return flow rate according to the total blood volume, Applicants believe the statements by the Examiner that Elgas also does not teach adjusting the blood removal or return rate underscore that each and every limitation of the claims is not disclosed in the combination of references and that a proper prima facie case for obviousness has not been met in this case. Furthermore, it is unclear how the Examiner believes Elgas reasonably provides motivation to one skilled in the art to modify Holmes in a manner different than what is actually taught in Elgas to arrive at the invention as presently claimed.

While some blood components, such as platelets, are collected by the device in the present invention, the subject's overall blood volume is not affected by the adjusting of the removal flow rate or return flow rate, and the present invention does not utilize the administration of outside fluids or medication to correct a decrease in blood volume. Instead, the present invention uses the total blood volume information of the subject as a basis for altering the blood removal flow rate or return flow rate to maintain proper

pressure in the blood vessel. In Elgas, the concern is an overall decrease in blood volume, such as critical blood loss during surgery. Because blood and fluid has been lost from the patient, blood or another fluid must be added from an outside source to replace the lost fluid. Accordingly, it is not clear how adjusting the blood removal flow rate or return flow rate for the heart-lung machine in Elgas would be capable of replacing the lost blood or other fluid. Since the heart-lung machine in Elgas oxygenates the blood for the patient during the surgery, stopping or significantly slowing down the heart-lung machine could be catastrophic to the patient. Thus, the methods of adjusting the removal flow rate or return flow rate during operation of the blood processing procedure as required by the present claims are wholly unsuitable for the blood volume problem faced in Elgas, and could even result in the death of the patient.

Likewise, the methods taught and suggested by Elgas are not suitable for the problem addressed by the present invention, i.e., preventing blood vessel infiltration due to pressure changes in the accessed blood vessel during the removal or return of blood. If the localized pressure in the blood vessel where blood is being removed or returned is too low or too high, then administering an outside fluid to adjust the subject's overall blood volume would not address the problem and could even worsen the problem. For example, if the pressure in an accessed blood vessel needs to be reduced to prevent rupturing the vessel, then introducing an additional fluid would serve no purpose whatsoever and may magnify the risk of infiltration by further increasing the blood vessel pressure. Administering an outside fluid to the patient is not related to the blood removal flow rate or return flow rate of the device and would not arrive at the present invention if combined with Holmes. If anything, administering fluids to the patient as taught by Elgas, thereby increasing the total blood volume, would make the device unsuitable for its intended purpose (MPEP 2141.02 and MPEP 2143.01).

Elgas and the present invention address two different and distinct problems in two substantially different ways. There is no reason in Holmes or the present invention to significantly increase the total blood volume. Furthermore, the methods disclosed in Elgas, i.e., administering an IV fluid or blood transfusion, would not address the

problems addressed by the present claims. Accordingly, one skilled in the art would not rationally modify the methods from Elgas and combine them with the methods of Holmes to arrive at the present invention. As a result, this ground of rejection under 35 U.S.C. 103(a) lacks the required articulated reasoning with rational underpinning under In re Kahn and MPEP 2141-2144 and should be withdrawn.

2. Claims 1, 11 and 23 drawn to "systematically" varying the flow rates

The Examiner further asserts that dependent claims (claims 1, 11 and 23) which recite "systematically varying" and "systematically decreasing" the removal flow rate or return flow rate are not patentable because Holmes discloses an apheresis system which varies the flow rates based on a predetermined operating scheme (page 3, lines 18-21, of the January 18th Office Action). Since the blood processing system of Holmes controls the operations, the Examiner considers the flow rates of Holmes to be "systemic" variations corresponding to the present claims (page 3, line 21, through page 4, line 2, of the January 18th Office Action).

This ground for rejection is erroneous because the Examiner has failed to interpret the claims according to the definitions provided in the specification. Page 19, lines 8-12, of the specification defines "systematically varying" as being varied by "substantially linear variations, exponential variations, logarithmic variations, quadratic variations." Each of these terms is also expressly defined on pages 16-18 of the specification. Thus, the term "systematically varying" and "systematically decreasing" do not mean variations controlled by the apheresis system as interpreted by the Examiner, but instead refer to variations that are substantially linear, exponential, logarithmic or quadratic.

Applicants can be their own lexicographers and are free to define "systematically" however they want as long as the term is not given meaning repugnant to the usual meaning of the term (MPEP 608.01(o)). The Examiner's adoption of another definition

of "systematically" cannot be sustained in view of the express language of the specification. This ground of rejections should therefore be withdrawn.

3. Further grounds of rejection for claims 3, 8, 9 and 10

Claims 3, 8, 9 and 10 ultimately depend from independent claim 27. Taken with the limitations of claim 27, these claims recite that the blood return flow rate decreases over the return time, decreases exponentially, decreases substantially in an exponential manner, or increases over the return time based on the determined total blood volume. The Examiner states that Holmes teaches total blood volume may be utilized to determine some parameters associated with the apheresis procedure (column 56, line 61, through column 57, line 6, of Holmes). The Examiner concludes that because the blood transfer rates of Holmes are determined by the operating parameters and that total blood volume can be utilized in some form to determine some of the parameters, the variable blood return flow rates in claims 3, 8, 9 and 10 are the result of mere optimization of a result-effective variable under MPEP 2144.05, the adjustment of which does not patentable distinguish over the prior art of record (page 5, lines 8-20, of the January 18th Office Action).

Applicants believe this ground of rejection is in error. Holmes does not disclose how or what parameters may utilize total blood volume, and there is no disclosure or suggestion in Homes that the blood return flow rate or removal flow rate are parameters that might be influenced by the total blood volume. Therefore the teaching in Holmes provides no clear correlation between total blood volume and adjusting blood return flow rate or removal flow rate to achieve a desired result. MPEP 2144.05, which forms the basis for this ground of rejection, requires that:

> "A particular parameter must first be recognized as a result effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of such variable might be characterized as routine experimentation. In re Antoine, 559 F.2d 618, 195 USPQ 6 (CCPA 1977)"

The cited references, including Holmes and Elgas, have not recognized that blood return flow rate and removal flow rate can be beneficially varied according to total blood

volume of the patient. Thus, total blood volume has not been recognized as a result effective variable which achieves a recognized result, such as the adjusted blood removal flow rate and blood return flow rate required by the present claims. Accordingly the requirements of MPEP2144.05 have not been met.

This argument was raised previously in the Response to Office Action file by Applicants on November 14, 2007. In response to Applicants' arguments that total blood volume has not been recognized as a result-effective variable which achieves a recognized result, the Examiner stated that Elgas discloses adjustment of total patient fluid volume via IV infusion as well as a variable speed pump that removes fluid from the patient (page 13, lines 6-10, of the January 18th Office Action). The Examiner therefore concludes that fluid removal rate may be used to control patient fluid volume and that taken together the references suggest that manipulation of fluid removal or return rates are variables able to control patient fluid volume when manipulated (page 13, lines 10-15, of the January 18th Office Action). As discussed above, this is based on a factual error. The variable speed pump in Elgas relied upon by the Examiner is used to transport blood from a reservoir to an oxygenation unit after the blood has already been removed from the patient by a separate cardiac pump (column 2, lines 40-48, of Elgas). The variable speed pump is not used in Elgas to remove blood from the patient. Thus there is no teaching in Elgas (or Holmes) that the blood removal rate or return rate of the device can be adjusted in order to manipulate or correct total blood volume. Furthermore, as discussed above, the adjusted blood return flow rate and removal flow rate of the present invention do not alter the total blood volume of the patient as taught by Elgas. Any corrections to the blood volume in Elgas are achieved through administration of an outside fluid. Instead, the present invention uses the total blood volume information of the subject as a basis for altering the blood removal flow rate or return flow rate to maintain proper pressure in the blood vessel.

Absent some correlation in the prior art between total blood volume and the desired adjustment of the blood removal flow rate or return flow rate of the present invention, which the Examiner has not provided, it cannot be said that these claims

represent a routine optimization of a result-effective variable. Accordingly, this ground of rejection should be withdrawn.

4. Further grounds of rejection for claims 4-7, 30-31 and 34-39

Claims 4-7, 30-31 and 34-39 ultimately depend from independent claim 27 and recite blood return flow rates and removal flow rates according to specific equations. As discussed in the preceding argument above, the Examiner asserts that Holmes discloses that the flow rate is recognized to be a result-effective variable and these claims merely set or optimize flow rates via the selection of variable parameters (page 6, lines 1-3, of the January 18th Office Action). The Examiner considers the selection of such variable parameters to be mere optimization of a result-effective variable through routine experimentation and not patentably distinct under MPEP 2144.05 (page 6, lines 3-10, of the January 18th Office Action).

As discussed above, this ground of rejection should be withdrawn because Holmes and Elgas do not disclose that the blood transfer rate is a parameter that utilizes total blood volume. As a result there is no support that total blood volume has been recognized as a result effective variable which achieves a recognized result, namely adjusting blood removal flow rate or blood return flow rate required by the present claims. Additionally, there is no suggestion or indication in the references that the specific equations recited by these claims would be predictable to one skilled in the art. Accordingly, the requirements of MPEP2144.05 have not been met and this ground of rejection should be withdrawn.

5. Rejection of claims 59-62 and 68 under 35 U.S.C. §103(a) as being obvious over Holmes in view of Elgas, further in view of Pierce

The Examiner also rejects claims 59-62 and 68 under 35 U.S.C. §103(a) as being obvious over Holmes in view of Elgas, further in view of Pierce. Pierce describes a blood processing procedure and device where blood is removed from a donor,

recirculated through the device, and the desired blood components separated and collected.

With regards to claims 59-62 and 68, which disclose specific equations for determining the proper blood fraction for collection based, in part, on cycle duration and the hematocrit ratio between the removed blood and recirculated blood, the Examiner states that each portion of blood necessarily has a hematocrit value, and that the draw and return cycles of Holmes and Pierce have a rate (page 11, lines 12-17, of the January 18th Office Action). The Examiner further asserts that all of the values used in the equations are demonstrated by the prior art to be variable and concludes these claims are merely the optimization of a result-effective variable under MPEP 2144.05 (page 11, lines 17-20, of the January 18th Office Action).

As stated above, MPEP 2144.05 requires a parameter must first be recognized as a result effective variable which achieves a recognized result before the determination of the optimum or workable ranges of such variable might be characterized as routine experimentation. The mere fact that the equations in claims 59-62 and 68 contain variables does not render the claims mere optimizations of a result-effective variable. There still must be a recognized nexus or correlation between the variables and the desired result (i.e., determining the fraction to be collected containing the desired blood component). It is not clear which variable the Examiner believes achieves the desired recognized result. Pierce discloses that the hematocrit values can be determined from the flow considerations, but there is no teaching that the hematocrit values can be altered by the process in Pierce, or that cycle duration times can be adjusted or modified based on the hematocrit values for the removed blood and recirculated blood. Other than the observation that the equations in claims 59-62 and 68 rely on multiple variables, the Examiner has provided no support or direction that the equations are the result of a variable able to achieve a recognized result required under MPEP 2144.05. Accordingly, the requirements of MPEP 2144.05 have not been met and this ground of rejection should be withdrawn.

Conclusion

Applicants believe the above arguments demonstrate that the Examiner has failed to make a proper prima facie case of obviousness under 35 U.S.C. §103. Even if combined, the references cited by the Examiner do not produce the limitations of the independent claims, namely adjusting the blood flow removal rate and return rate during operation of the blood processing procedure based on the patient's total blood volume. Additionally, the Examiner has not provided any articulated reasoning with supportable rational underpinning that would explain why one skilled in the art would modify Elgas, which teaches administering outside fluids to correct a loss of total blood volume, to encompass adjusting the blood removal rate or return rate of the blood processing procedure and then combine this modified procedure with Holmes. Furthermore, the Examiner has not shown that the variables in the dependent claims are recognized as result effective variables which achieve recognized results as required under MPEP 2144.05.

A decision withdrawing the pending rejections and allowing the pending claims is therefore respectfully requested.

This amendment is accompanied by a Petition for Extension of Time (one month) and payment in the amount of $120.00 as required under 37 C.F.R. 1.17. The fee set forth in 37 C.F.R. 41.20(b)(2) in the amount of $510.00 is also provided. If the amount submitted is incorrect, however, please deduct from Deposit Account No. 07-1969 the appropriate fee for this submission and any extension of time required.

Respectfully submitted,

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VIII. CLAIMS APPENDIX

1. (rejected) The method of claim 27, further comprising the step of: systematically varying said return flow rate over said return time.

2. (rejected) The method of claim 1 wherein said return flow rate decreases over said return time.

3. (rejected) The method of claim 1 wherein said return flow rate decreases in a substantially linear manner over said return time.

4. (rejected) The method of claim 3 wherein said return flow rate is provided by the expression:

$Z_{ret} = [F_0 + 2(1- F_0)(t/t_r)] Q_{ret}$;

wherein Z_{ret} is said return flow rate, t is time, F_0 has a value greater than 1 and less than or equal to 2, t_r is said return time and Q_{ret} is an average return flow rate.

5. (rejected) The method of claim 4 wherein Q_{ret} is selected such that the extent of hemolysis during blood processing is less than about 0.1%.

6. (rejected) The method of claim 4 wherein Q_{ret} is a value selected from the range of about 50 ml min^{-1} and about 400 ml min^{-1}.

7. (rejected) The method of claim 4 wherein t_r is a value selected from the range of about 0.5 min to about 0.9 min.

8. (rejected) The method of claim 1 wherein said return flow rate decreases exponentially over said return time.

9. (rejected) The method of claim 1 wherein said return flow rate decreases in a substantially exponential manner over said return time.

10. (rejected) The method of claim 1 wherein said return flow rate increases over said return time.

11. (rejected) The method of claim 1, further comprising the step of systematically varying said removal flow rate over said blood removal time.

12. (rejected) The method of claim 1 wherein said removed blood is removed through a needle and said return component is returned through said needle.

13. (rejected) The method of claim 1 wherein said removed blood is removed through a first access needle and said return component is returned through a second access needle.

14. (rejected) The method of claim 1 wherein said processing step comprises the steps of:

separating said removed blood into a plurality of separated blood components including at least one collect component and said return component; and

collecting a collect component.

15. (rejected) The method of claim 14 wherein said separating step comprises conducting said removed blood through a density centrifuge system.

16. (rejected) The method of claim 14 wherein said separating step comprises conducting said removed blood through a centrifugal elutriation system.

17. (rejected) The method of claim 14 wherein said collect component is plasma.

18. (rejected) The method of claim 14 wherein said collect component is red blood cells.

19. (rejected) The method of claim 14 wherein said collect component is white blood cells.

20. (rejected) The method of claim 14 wherein said collect component is platelets.

21. (rejected) The method of claim 1 wherein said blood is removed during a draw cycle and said portion of said return component is returned during a return cycle.

22. (rejected) The method of claim 21 further comprising the step of sequentially repeating said draw and return cycles for a selected blood processing time.

23. (rejected) The method of claim 27 further comprising the step of:
systematically decreasing said return flow rate during said return time, where said method reduces the incidence of an access blood vessel infiltration during blood processing.

24. (rejected) The method of claim 27, further comprising the step of:
sequentially repeating said steps of removing blood and of returning blood for a selected blood processing time, whereby the removal flow rate is increased each draw cycle by a selected flow adjustment increment.

25. (rejected) A method of processing blood, comprising the steps of:

determining the total blood volume of a subject undergoing a blood processing procedure;

removing blood from said subject at a selected removal flow rate thereby generating removed blood, wherein said selected removal flow rate is adjusted during operation of the blood processing procedure based on said total blood volume;

processing said removed blood, thereby generating processed blood including at least one return component; and

returning at least a portion of said return component to said subject at a return flow rate.

26. (rejected) A method of processing blood, comprising the steps of:

determining the total blood volume of a subject undergoing a blood processing procedure;

removing blood from said subject, thereby generating removed blood;

processing said removed blood, thereby generating processed blood including at least one return component; and

returning at least a portion of said return component to said subject at a selected return flow rate, wherein said selected return flow rate is adjusted during operation of the blood processing procedure based on said total blood volume of said subject.

27. (rejected) A method of processing blood, comprising the steps of:

determining the total blood volume of a subject undergoing a blood processing procedure;

removing blood from said subject at a removal flow rate thereby generating removed blood, wherein said removal flow rate is adjusted during operation of the blood processing procedure based on said total blood volume;

processing said removed blood, thereby generating processed blood including at least one return component; and

returning at least a portion of said return component to said subject at a return flow rate, wherein said return flow rate is adjusted during operation of the blood processing procedure based on said total blood volume of said subject.

28. (rejected) The method of claim 27 wherein said return and removal flow rates are linearly correlated to said total blood volume of said subject.

29. (rejected) The method of claim 28 wherein said return and removal flow rates increase with increasing total blood volume of said subject.

30. (rejected) The method of claim 27 wherein said removal flow rate is provided by the expression:

$$Z_{rem} = (M_{rem}) \times (V_B) \leq Q_{rem\ max},$$

wherein Z_{rem} is the removal flow rate, M_{rem} is a removal flow rate slope, V_B is the total blood volume of said subject and $Q_{rem\ max}$ is a maximum removal flow rate.

31. (rejected) The method of claim 27 wherein said return flow rate is provided by the expression:

$$Z_{ret} = (M_{ret}) \times (V_B) \leq Q_{ret\ max}$$

wherein Z_{ret} is the return flow rate, M_{ret} is a return flow rate slope, V_B is the total blood volume of said subject, and $Q_{ret\ max}$ is a maximum return flow rate

32. (rejected) The method of claim 27 wherein said subject is a human male and said total blood volume is determined using the expression:

$$V_B = 604 + \left(3.669x10^{-4}\right)\left(L^3\right) + (32.187)(W),$$

wherein L is the length of the subject in units of centimeters, W is the weight of the subject in units of kilograms and V_B is total blood volume in units of milliliters.

33. (rejected) The method of claim 27 wherein said subject is a human female and said total blood volume is determined using the expression:

$$V_B = 183 + \left(3.561x10^{-4}\right)\left(L^3\right) + (33.069)(W),$$

wherein L is the length of the subject in units of centimeters, W is the weight of the subject in units of kilograms and V_B is total blood volume in units of milliliters.

34. (rejected) The method of claim 30 wherein M_{rem} is a value selected from the range of about 0.0066 min^{-1} and about 0.05 min^{-1} and $Q_{rem\ max}$ is a value selected from the range of about 100 ml min^{-1} to about 160 ml min^{-1}.

35. (rejected) The method of claim 34 wherein $Q_{rem\ max}$ is about 142 ml min^{-1}.

36. (rejected) The method of claim 31 wherein M_{ret} is a value selected from the range of about 0.025 min^{-1} and about 0.200 min^{-1} and $Q_{ret\ max}$ is a value selected from the range of about 200 ml min^{-1} and about 400 ml $min.^{-1}$.

37. (rejected) The method of claim 36 wherein $Q_{ret\ max}$ is about 302 ml $min.^{-1}$.

38. (rejected) The method of claim 30 wherein M_{rem} is provided by the expression:

$M_{rem} = (C_{qr}) \times (A_{rem})$

wherein C_{qr} is a selectably adjustable processing rate parameter, A_{rem} is a constant having a value selected from the range of about 0.01 min^{-1} to about 0.05 min^{-1} wherein the value of C_{qr} is selected to avoid the occurrence of infiltration of an access blood vessel of said subject.

39. (rejected) The method of claim 31 wherein M_{ret} is provided by the expressions:

$M_{ret} = (C_{qr}) \times (A_{ret})$,

wherein C_{qr} is a selectably adjustable parameter, A_{ret} is a constant having a value selected from the range of about 0.05 min^{-1} to about 0.20 min^{-1}, and wherein the value of C_{qr} is selected to avoid discomfort of said subject.

40. (rejected) The method of claim 27 wherein said removed blood is removed through an access needle and said return component is returned through said access needle.

41. (rejected) The method of claim 27 wherein said removed blood is removed through a first access needle and said return component is returned through a second access needle.

42. (rejected) The method of claim 27 wherein said blood is removed during a draw cycle and said portion of said return component is returned during a return cycle.

43. (rejected) The method of claim 42 further comprising the step of sequentially repeating said draw and return cycles for a selected blood processing time.

44. (rejected) The method of claim 27 wherein said processing step comprises the steps of:

separating said removed blood into a plurality of separated blood components including at least one collect component and said return component; and

collecting a collect component.

45. (rejected) The method of claim 44 wherein said separating step comprises conducting said removed blood through a density centrifuge system.

46. (rejected) The method of claim 44 wherein said separating step comprises conducting said removed blood through a centrifugal elutriation system.

47. (rejected) The method of claim 44 wherein said collect component is plasma.

48. (rejected) The method of claim 44 wherein said collect component is red blood cells.

49. (rejected) The method of claim 44 wherein said collect component is white blood cells.

50. (rejected) The method of claim 44 wherein said collect component is platelets.

51. (rejected) The method of claim 44, further comprising the steps of:

conducting said removed blood through a blood separation system, wherein said collect component comprises a first portion of said removed blood;

recirculating a second portion of said removed blood through said blood separation system; wherein said second portion corresponds to a recirculated component of said removed blood; and

returning a third portion of said removed blood to said subject during a return cycle, wherein said third portion corresponds to a return portion of said removed component;

wherein the fraction by volume of said removed blood comprising said collected component is selected to prevent contamination of said collect component with red blood cells.

52. (rejected) The method of claim 51 further comprising the step of sequentially repeating said draw and return cycles for a selected blood processing time.

53. (rejected) The method of claim 51 further comprising the step of adding an anticoagulant agent to said removed blood.

54. (canceled)

55. (canceled)

56. (rejected) The method of claim 51 wherein said blood separation system comprises a density centrifuge operationally connected to a centrifugal elutriation system.

57. (rejected) The method of claim 51 wherein said removed blood has a first hematocrit, H_{rem}, and said recirculated component has a second hematocrit, H_{recir}, and wherein the weighted average of the hematocrit of said removed blood and the hematocrit of said recirculated component is less than or equal to $\left(1-\left(\frac{H_{rem}}{H_{recir}}\right)\right)$.

58. (rejected) The method of claim 51 wherein the weighted average of the hematocrit of said removed blood and the hematocrit of said recirculated component is less than 70%.

59. (rejected) The method of claim 51 wherein said removed blood and said recirculated component are conducted through said blood processing system at a first rate, R_1, during said return cycle and wherein said removed blood and said recirculated component are conducted through said blood processing system at a second rate, R_2, during said draw cycle, wherein said removed blood has a first hematocrit, H_{rem}, and said recirculated component has a second hematocrit, H_{recir}, wherein t_{draw} is the duration of the draw cycle and t_{ret} is the duration of the return cycle, wherein the fraction by volume of said removed blood comprising said collected component, F_{cmax}, is provided by the equation:

$$F_{c\max} = \left(\left(\left[A^2 + \frac{(1-b)}{(1-D)} \right] 0.5 - A \right) \right),$$

wherein b is provided by the equation:

$$b = \frac{H_{rem}}{H_{recir}},$$

D is provided by the equation:

$$D = \frac{t_{draw}}{\left(t_{draw} + t_{ret} \right)},$$

A is provided by the equation:

$$A = \left(\frac{\left(\frac{1}{1-D} \right) + \left(\frac{C_r}{D} \right)}{2} \right),$$

and C_r is provided by the equation:

$$C_r = \left(\frac{R_{ret}}{R_{draw}} \right).$$

60. (rejected) The method of claim 59 wherein b is a value selected from the range of about 0.46 to about 0.85.

61. (rejected) The method of claim 59 wherein D is a value selected from the range of about 0.60 to about 0.73.

62. (rejected) The method of claim 59 wherein C_r is a value selected from the range of about 0.4 to about 0.6.

63. (rejected) The method of claim 51 wherein said collect component is platelets.

64. (rejected) The method of claim 51 wherein said collect component is plasma.

65. (rejected) The method of claim 51 wherein said collect component is white blood cells.

66. (rejected) The method of claim 51 wherein said collect component is white blood cells and platelets.

67. (rejected) The method of claim 51 wherein said removed blood is removed through an access needle and said return component is returned through said access needle.

68. (rejected) The method of claim 51 wherein said removed blood and said recirculated component are conducted through said blood processing system at a first rate, R_1, during said return cycle and wherein said removed blood and said recirculated component are conducted through said blood processing system at a second rate, R_2, during said draw cycle, wherein said removed blood has a first hematocrit, H_{rem}, and said recirculated component has a second hematocrit, H_{recir}, wherein t_{draw} is the duration of the draw cycle and t_{ret} is the duration of the return cycle, wherein V_{svn} is the volume of removed blood required to fill a fixed volume return reservoir and V_{svnr} is the volume of the recirculated component recirculated each draw and return cycle, wherein the fraction by volume of said removed blood comprising said collected component, F_{cmax}, is provided by the equation:

$$F_{c\max} = \left(\frac{\left(\left[A^2 + \frac{(1-z)(1-b)}{(1-D)} \right]^{0.5} - A \right)}{(1-z)} \right),$$

wherein b is provided by the equation:

$$b = \frac{H_{rem}}{H_{recir}},$$

D is provided by the equation:

$$D = \frac{t_{draw}}{\left(t_{draw} + t_{ret} \right)},$$

A is provided by the equation:

$$A = \left(\frac{\left(\frac{1}{1 - D} \right) + \left(\frac{C_r}{D} \right)}{2} \right),$$

C_r is provided by the equation:

$$C_r = \left(\frac{R_{ret}}{R_{draw}} \right), \text{ and}$$

z is provided by the equation

$$z = \left(\frac{V_{svnr}}{V_{svn}} \right).$$

IX. EVIDENCE APPENDIX

No evidence under 37 C.F.R. 1.130, 1.131 or 1.132 is being relied upon or submitted.

X. RELATED PROCEEDINGS APPENDIX

There are no prior or pending appeals, interferences or judicial proceedings that are related to the pending appeal.